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Prenatal coverage of experimental gastroschisis with a collagen scaffold to protect the bowel

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Abdominal wall defect;
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Gastroschisis;
Tissue engineering

Abstract

Background/Purpose: In fetuses with gastroschisis, toxic products in the amniotic fluid and constriction at the defect of the abdominal wall are considered causative of damage to the eviscerated bowel. The aim of this study was to cover the eviscerated bowel in gastroschisis with a collagen scaffold to protect the bowel and induce cell growth into the scaffold, which could lead to skin or abdominal wall formation replacing the scaffold.

Methods: In 12 fetal lambs gastroschisis was surgically created at 79 days gestation. A dual-layer type I collagen scaffold was sutured into the skin of the abdominal wall around the defect covering the eviscerated bowel. Lambs were examined after caesarean section at 140 days' gestation.

Results: Survival was 67%. In 7 of 8 surviving lambs the bowel was found to be covered after birth. One scaffold had ruptured. The bowel was found repositioned in the abdominal cavity in 5 lambs. In 2 lambs it was still partially outside. Only minor adherence of bowel loops and no fibrous peel formation were seen. Connective tissue and skin tissue replaced the scaffold.

Conclusions: Prenatal coverage of the bowel in experimental gastroschisis with a collagen scaffold is feasible in fetal lambs, significantly diminished damage to the bowel wall, and skin and connective tissue replaced the scaffold. This technique may be promising in the care of fetuses with this congenital anomaly.

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Gastroschisis is an abdominal wall defect, resulting in herniation of a large part of the bowel outside the abdominal cavity, where it is in direct contact with the amniotic fluid.

Mortality in neonates with gastroschisis is reported to be 4%–12.5%. Intra-uterine growth retardation and premature birth are frequently noted, and serious complications like sepsis, bowel dysfunction, bowel atresia, bowel necrosis and subsequent short bowel syndrome may occur. Intestinal motility and absorption are decreased and postnatal feeding can be problematic [1–4]. At birth, the bowel is often covered with an inflammatory fibrous peel, and bowel loops are matted together, can be congested or ischemic, and are thickened, inflamed and edematous. This damage to the eviscerated bowel may be the result of constriction at the site of the abdominal wall defect and/or the toxic effect of the amniotic fluid [5,6]. Damage to the bowel seems to occur during the last trimester of pregnancy, when the bowel is growing, causing compression at the site of the abdominal wall defect. Additionally, the composition of amniotic fluid is changing due to the improving kidney function and the release of gastrointestinal waste products into the amniotic fluid [7–11]. Primary closure of the abdominal wall can be problematic because the abdominal cavity is relatively hypoplastic and the bowel volume is enlarged due to edema and fibrous peel formation (visceral-abdominal disproportion). Repositioning the bowel into the abdominal cavity will increase the intra-abdominal pressure, and may result in respiratory problems, compromised venous blood flow and abdominal compartment syndrome. In these cases a gradual abdominal wall closure with a spring-loaded silo is often employed. [12]. Occasionally prosthetic materials are needed to close the abdominal wall or the fascia defects. These materials may also cause complications, including wound infection, bowel fistula, erosion into abdominal viscera, lack of fixation, mesh extrusion and extreme adhesion formation [13]. Furthermore, patch dehiscence may occur because the material does not grow with the child [14].

Tissue engineered constructs can be useful for the operative closure of these defects, either prenatal or in the neonatal period. A carrier material of extracellular matrix is provided to the tissue. Cell ingrowth into this scaffold, replacing and degrading the scaffold, will result in newly formed or regenerated autologous tissue. We developed a molecularly defined, biocompatible, acellular, single or dual-layer porous scaffold from type I collagen derived from bovine Achilles-tendon [15–17]. In previous animal research this collagen scaffold was used to augment the bladder [18], repair fetal skin defects [19], and close a full-thickness abdominal wall defect [20].

Routine ultrasound screening during pregnancy allows early detection of gastroschisis, and offers the potential option for early treatment during the fetal period, to protect the bowel from secondary injury [21].

The purpose of this study was to evaluate the protective effect of intra-uterine coverage of the eviscerated bowel tissue in fetal lambs in which gastroschisis was surgically created, aiming at preventing fibrous peel and adhesion formation. For this purpose we used the previously used dual-layer collagen scaffold. Findings were compared to a historical control

group of lambs, from a previous study, in which the eviscerated bowel was left uncovered [20]. Additionally, we aimed at inducing cell ingrowth into the scaffold, ultimately resulting in skin or abdominal wall tissue replacing the scaffold and covering the vulnerable bowel loops.

1. Materials and methods

The study was conducted under the supervision of veterinarians according to National Institutes of Health (NIH) guidelines for the care and use of laboratory animals (NIH publication 85-23 Rev. 1985). The study was approved by the Ethical Committee on Animal Research of the Radboud University Nijmegen Medical Centre.

1.1. Preparation of collagen scaffolds

Molecularly-defined, biocompatible and biodegradable dual-layer collagen scaffolds were made from insoluble, highly purified, type I collagen from bovine Achilles tendon [15–17]. The scaffold consisted of a porous layer and a dense film layer. The preparation and characterisation of this scaffold were previously described [20].

Before implantation the scaffolds were disinfected in 70% (v/v) ethanol and washed with sterile phosphate-buffered saline (PBS).

1.2. Surgical procedures

Twelve pregnant sheep (Dutch Texel breed) were operated at 79 days' gestation (full term 140–147 days). Anesthesia was induced by pentobarbital (30 mg/kg intravenous, AST Pharma, Oudewater, The Netherlands) and atropine sulphate (1 ml intravenous, Pharmachemie BV, Haarlem, The Netherlands) and, following endotracheal intubation, maintained with 2% isoflurane (Nicholas Piramal, London, UK) and O₂/air ventilation at a respiration rate of 16 per min. Heart rate, temperature, oxygen saturation and carbon dioxide concentration of the expired air were monitored. The abdomen was shaved, cleaned and aseptically prepared. A lower midline abdominal incision was made. One horn of the uterus was exteriorized, and wrapped in gauze soaked in warmed PBS. A hysterotomy was performed and the lower part of the fetal body was exposed. In case of twin or triplet pregnancy only one fetus was operated to avoid additional risk of complications.

In 12 fetuses (5 male, 7 female), gastroschisis was surgically created as previously described [20]. An incision of 2.5 cm through skin, fascia, muscle and peritoneum was made in the left lower quadrant of the abdominal wall, resulting in a full-thickness abdominal wall defect of approximately 2.5 × 2 cm. The defect was created on the left side to avoid injury to the liver. The bowel was exposed and gently extruded from the abdominal cavity, to create a gastroschisis-like lesion. Subsequently the skin around the

defect was ovally incised at approximately 3 mm from the edges of the defect. The skin edges of this oval wound were carefully detached from the underlying fascia (Fig. 1A). The dual-layer collagen scaffold, measuring approximately 3×3.5 cm was placed into this oval skin defect (film layer at the intestinal site), covering the eviscerated bowel. The scaffold was sutured to the skin and the abdominal wall with 6-0 polyglecaprone (Monocryl®, Ethicon Inc.; Sommerville, NJ, USA) running sutures (Fig. 1B+C). Four 6-0 polypropylene (Prolene®, Ethicon Inc.; Sommerville, NJ, USA) marking sutures were placed around the scaffold for future reference.

After the surgical procedure the fetus was returned into the uterus and amniotic fluid volume was restored with warmed sterile PBS together with Amoxicillin (250 mg, Centrafarm Services B.V., Etten-Leur, The Netherlands). The uterus was closed in two layers with a 2-0 polyglactin (Vicryl®, Ethicon Inc.; Sommerville, NJ, USA) running suture. Sodium-penicillin (1,000,000 IU, Astellas Pharma, Leiderdorp, The Netherlands) was instilled into the intra-abdominal space and the maternal laparotomy was closed in two layers using 1 polyglactin interrupted suture. Depomycin (20,000 IU penicillin ml⁻¹, streptomycin ml⁻¹, 20 mg/kg, subcutaneous, Intervet, Boxmeer, The Netherlands) was initiated preoperatively and maintained postoperatively for three days.

At 140 days' gestation, 61 days after fetal surgery, the lambs were delivered by caesarean section under local anaesthesia with Lidocaine 2% (20–30 ml, subcutaneous and intramuscular, Fresenius Kabi, Den Bosch, The Netherlands).

1.3. Neonatal outcome and evaluation

After birth, the regenerated part of the abdominal wall at the site of the incorporated scaffold was macroscopically observed, palpated, measured and photographed. Subsequently the lambs were sacrificed with medetomidine (0.5 mg, intramuscular, Orion pharma, Espoo, Finland) and pentobarbital (60 mg/kg, intracardial).

The abdominal wall of the lambs was opened with broad margins around the site of the former scaffold. The intra- and extra-abdominal parts of the bowel were evaluated for adhesions and fibrous peel formation. The abdominal wall and the bowel, from pylorus to rectum, were taken out.

1.4. Histological staining

Tissue samples were taken from the bowel situated outside the abdominal cavity and from bowel inside the abdominal cavity. Additionally, tissue samples were taken from the regenerated tissue at the site of the implanted collagen scaffold and from the bowel lying underneath the site of the implanted collagen scaffold.

The tissue samples were fixed in 10% (v/v) buffered formalin and paraffin-embedded for routine histological processing. Sections (4 µm) were cut and stained with haematoxylin and eosin and Masson's trichrome. The intestinal tissue was examined for changes in the mucosal, submucosal, muscle and serosal layers, and fibrous peel and adhesion formation. Two bowel samples from each fetus were used to assess the thickness of the muscularis propria and the serosa with fibrous peel layer (if present) in three random fields using an ocular micrometer at 100× magnification. The specimens which included the site of the implanted collagen scaffold were examined for evidence of epithelialization, neovascularization, smooth muscle cell ingrowth, signs of inflammation, and degradation of the scaffold.

1.5. Data analysis

Data analysis of the bowel measurements was performed with SPSS 16.0 for Windows (SPSS, Chicago, USA), and expressed as mean±standard deviation. Statistical analysis was performed using the independent samples t-test for equality of means. *P* < .05 was considered statistically significant.

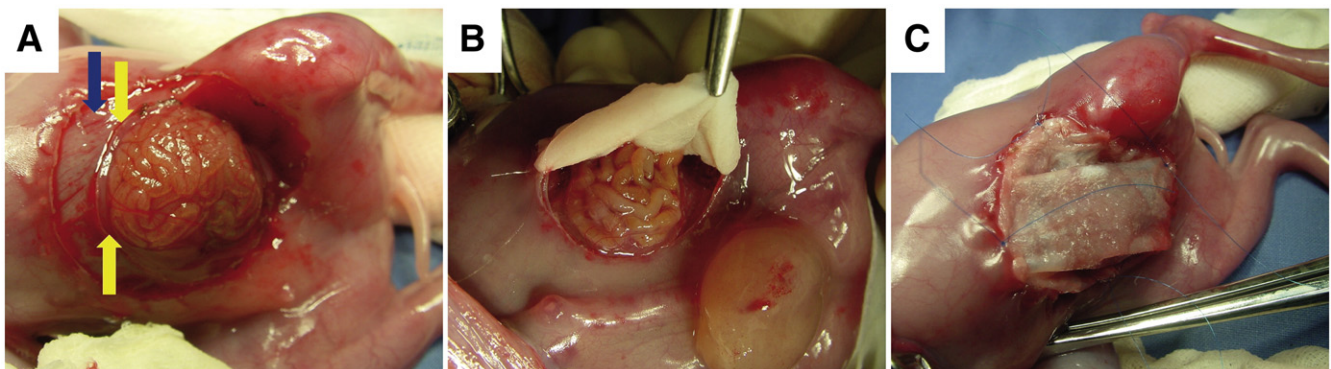


Fig. 1 Surgery on fetal lambs at 79 days gestation. (A) Surgically created gastroschisis; blue arrow: oval incision of skin around defect; yellow arrows: skin between incision and defect. (B) Gastroschisis partially covered with collagen scaffold. (C) Gastroschisis completely covered with collagen scaffold.

Table 1 Characteristics of operated lambs after birth.

Lamb	Location bowel	Complications
1	Intra-abdominal	-
2	Intra-abdominal	-
3	Intra-abdominal	-
4	Intra-abdominal	-
5	Intra-abdominal	Obstructive ileus
6	Largely extra-abdominal	-
7	Small part extra-abdominal	-
8	Extra-abdominal	Gastroschisis

2. Results

2.1. Animal surgery

Eight of the 12 operated fetuses were born alive (overall survival 67%). Two fetal abortions occurred, one with no distinct reason, one due to a torsion of the eviscerated bowel. Two pregnant ewes were euthanised because of fascial dehiscence 3 weeks after operation. No additional maternal deaths occurred.

2.2. Macroscopic Results

After birth, 5 lambs presented with a closed abdominal wall and all bowel loops inside the abdominal cavity (lambs 1–5). Two lambs had a partially extra-abdominal bowel which was covered with regenerated skin tissue that replaced the scaffold (lambs 6 and 7). In lamb 8 the scaffold had ruptured and the eviscerated bowel was covered with fibrous peel and very coalescent, like in (lambs with) untreated gastroschisis. An overview of characteristics is given in [Table 1](#).

Lambs 1–5 presented with a closed abdominal wall, the bowel was entirely inside the abdominal cavity. From the marking sutures inwards, first normal appearing skin tissue with hair growth was visible. In the centre of the regenerated tissue hyperkeratotic tissue was seen ([Fig. 2A](#)), and in 2 lambs a small central dry ulcer was found. In 4 of these 5 lambs the bowel showed no abnormalities, and only some minor adhesions to the abdominal wall were seen ([Fig. 2B](#)). In the other lamb (lamb 5) we saw massive adhesions between bowel loops and with the abdominal wall ([Fig. 2C](#)). The proximal bowel loops were very dilated. Dissection revealed a small loop with stenosis, which was the cause of

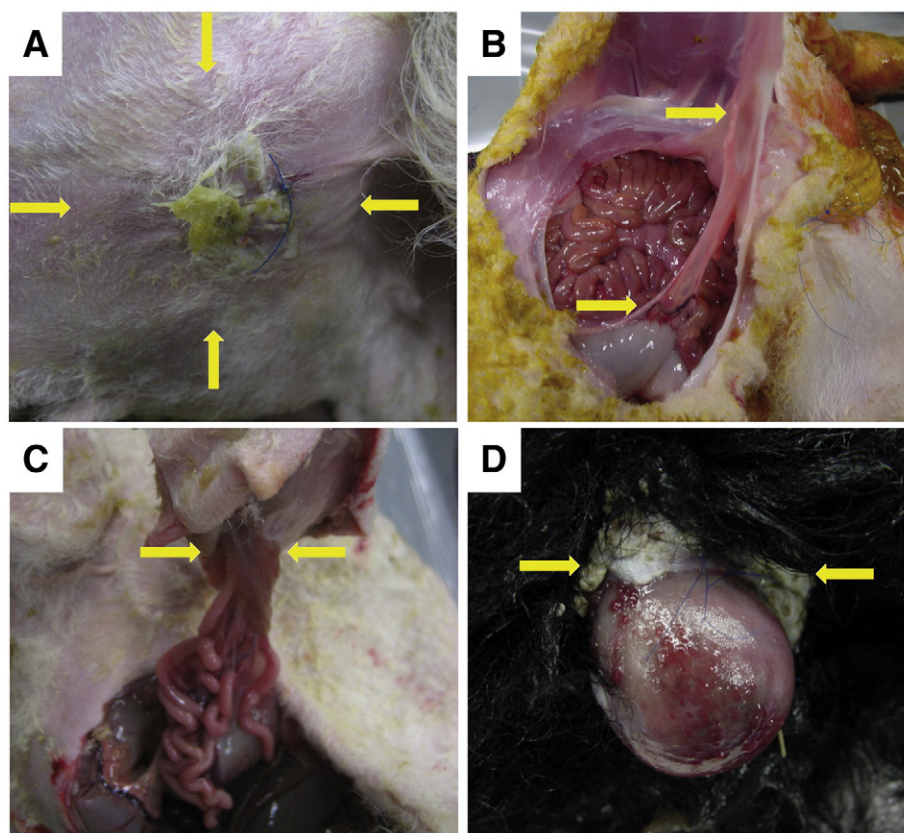


Fig. 2 Macroscopic aspects after birth (lambs 1–5 and 8) (A) Showing regenerated skin-like tissue (between arrows) and central hyperkeratinisation. (B) Minor adhesions after opening the abdominal wall. (C) Lamb 5 in which bowel loops were very adhesive, arrows pointing at former defect in abdominal wall. (D) Lamb 8 in which an uncovered gastroschisis was found; bowel loops were covered with fibrous peel and adhesive. Arrows pointing at remnants of scaffold.

the obstructive ileus in this lamb. In all these 7 lambs the skin edges that surrounded the former defect, situated between the area where the scaffold was sutured to the skin and the abdominal wall defect, had formed epidermal inclusion cysts.

Of the 2 lambs in which the bowel was partially outside the abdominal wall, lamb 6 presented with a large extent of extra-abdominal bowel, measuring $7 \times 8 \times 2$ cm (length \times width \times height) in size. The bowel was covered with skin tissue and appeared to be in a subcutaneous pocket. The skin appeared normal, even with hair growth, with the exception of a small central area (Fig. 3A). The bowel was enveloped in a sac of peritoneum which was adhesive to the skin of the abdominal wall (Fig. 3B). A 2 cm defect in the abdominal wall was palpable. The extra-abdominal bowel

had some minor adhesions, no adhesions were seen inside the abdomen (Fig. 3C+D). Lamb 7 presented with less extra-abdominal bowel, measuring $3.5 \times 2 \times 1$ cm. The centre of the regenerated skin, which covered the bowel, was hyperkeratotic, and the surrounding tissue had a ridged configuration (Fig. 3E). The extra-abdominal bowel showed moderate adhesions, but the intra-abdominal bowel was without adhesions (Fig. 3F). In both lambs no fibrous peel formation was seen on the bowel.

Lamb 8 had a rupture of the scaffold, uncovering the eviscerated bowel. The bowel loops were very coalescent, and showed extensive adhesions and fibrous peel formation (Fig. 2D). Inside the abdomen only minor adhesions were observed. Remnants of the scaffold were visible on the abdominal wall.

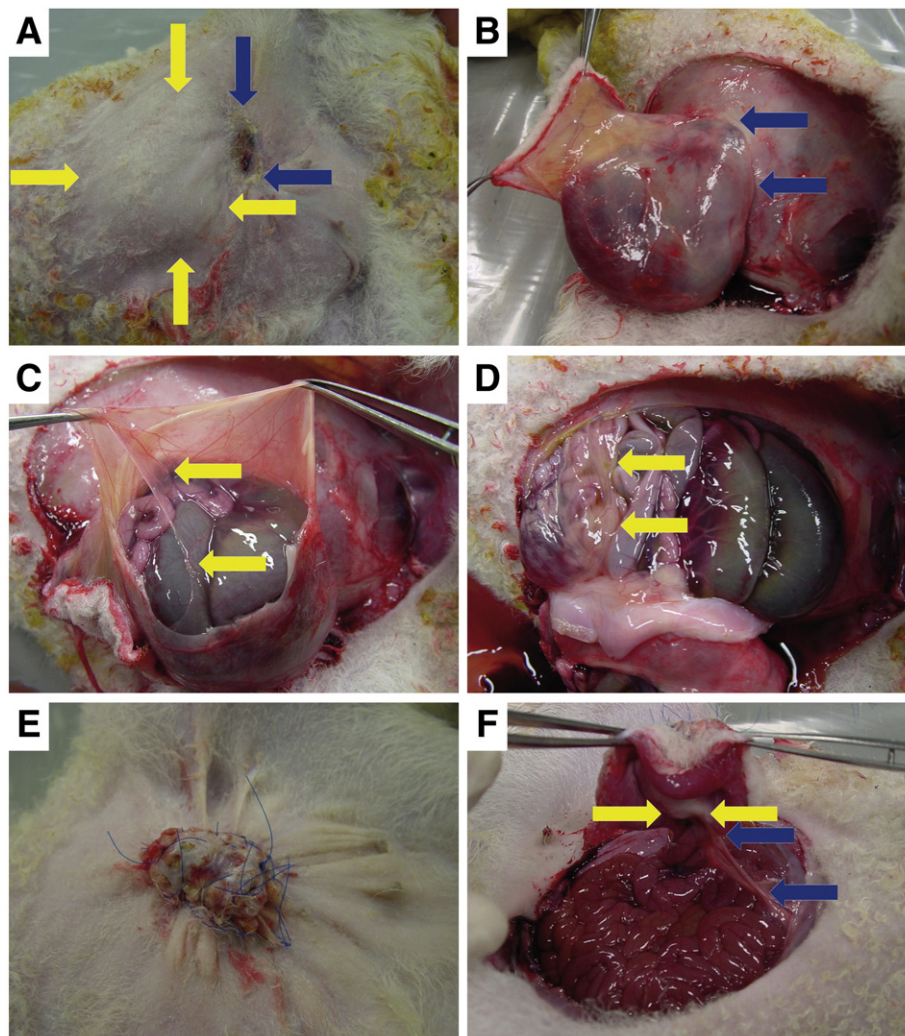


Fig. 3 Macroscopic aspects after birth (lambs 6 and 7). (A) Covered gastroschisis in lamb 6. The skin is bulging (yellow arrows) caused by the subcutaneous, partially extra-abdominal, bowel loops. Less mature skin tissue at centre of newly formed tissue (blue arrows). (B) After opening the skin tissue, bowel loops enveloped in peritoneum were visible. Defect in the abdominal wall between blue arrows. (C) After opening of the peritoneal sac bowel loops were seen, and had only slight adhesions (yellow arrows). (D) Intra-abdominally only slight adhesions (yellow arrows) were found as well. (E) Lamb 7 presented with only a small part of bowel outside the abdominal wall, hyperkeratotic tissue was covering the bowel. (F) After opening the skin, the defect in the abdominal wall was visible (between yellow arrows), and only slight adhesions of the bowel were observed (blue arrows).

2.3. Histological results

2.3.1. Bowel tissue

Normal historical control lambs in our previous study had a serosa of 0.02 ± 0.01 mm and an intestinal muscularis of 0.08 ± 0.03 mm [20].

In lambs 1–6 no histological abnormalities of the bowel tissue were observed. No fibrous peel formation was found, the serosal layer (0.04 ± 0.04 mm) and the intestinal muscularis (0.05 ± 0.02 mm) showed no statistical significant difference in thickness compared to control lambs ($P=.09$ and $P=.07$ respectively). The submucosa and mucosa appeared normal (Fig. 4A). In lamb 7 ischemic necrosis with hemorrhagic infarction was present in the bowel loop with stenosis, and necrosis of the mucosa was observed. In lamb 8 the serosa of the eviscerated bowel was covered with fibrous peel, (0.37 ± 0.05 mm) consisting of deposits of fibrin, degenerated granulocytes and granulation tissue. The fibrous peel was covered with a pseudo-epithelial mesenchymal layer of cells, which seemed to protect the bowel tissue against the amniotic fluid (Fig. 4B). Neither prominent inflammation, nor edema, venous dilatation, lymphatic dilatation or signs of ischemia in the bowel tissue were seen. The mucosa appeared normal, with normal slender villi, and the submucosa was normal, without collagen deposits. The intestinal muscularis was not thickened (0.06 ± 0.02 mm), but did show collagen deposition; ganglion cells were normal.

2.3.2. Abdominal wall tissue

In all lambs, histological examination of the abdominal wall tissue covering the original defect showed that the porous layer of the collagen scaffold was replaced by connective tissue consisting of collagen and fibroblasts. There was a firm connection with the adjacent skin and subcutaneous tissue of the native abdominal wall. In all lambs, the exterior side of the regenerated tissue was covered with skin tissue. The newly formed skin tissue was more mature at the edges, with epithelialization and appendages including sebaceous glands and hair follicles, compared to

the centre (Fig. 5A–D). Hyperkeratinization was visible at the centre of this tissue, with a hyperplastic epidermis underneath (Fig. 5A+D). Tissue regeneration seemed to occur from the borders of the native tissue to the centre of the newly formed tissue. Neovascularization was seen throughout the entire regenerated tissue. Only a minor chronic inflammatory reaction was observed. The collagen scaffold was largely degraded, except for the less-porous film layer, which was still visible at the inside of the regenerated tissue. In 2 lambs a small ulcer was found, which showed remnants of the scaffold, fibrin deposition, granulocytes and necrosis.

3. Discussion

The mortality rate in gastroschisis patients is reported to be 4%–12.5%, but postnatal complication rates up to 79% have been reported [1–4]. Damage to the bowel is proposed to occur during late pregnancy, due to constriction of the bowel at the site of the abdominal wall defect and exposure to the amniotic fluid [5]. Gastroschisis can be detected in early pregnancy [15], which offers the potential option to salvage the bowel tissue with fetal therapy.

Stephenson et al. repaired an experimental gastroschisis in sheep 25 days after creation, by replacing the bowel into the abdomen and subsequent surgical closure of the abdominal wall. They reported reversal of damage to the bowel visible at 100 days of gestation, with a normal appearance of the bowel at term (135 days) [22]. Langer et al. surgically created a gastroschisis in fetal lambs at 80 days of gestation, and performed repair at 120 days of gestation, involving relief of bowel constriction and coverage of the eviscerated bowel with a silastic sheet. In the repair group a partial reversal of damage to the bowel was observed at histological evaluation and in bowel contractility studies after birth [6].

In previous work, we used this fetal lamb model for gastroschisis, and performed an immediate repair by suturing the same collagen scaffold as was used in the present study into the abdominal wall defect. Instead of leaving the eviscerated bowel out of the abdominal cavity, as in the

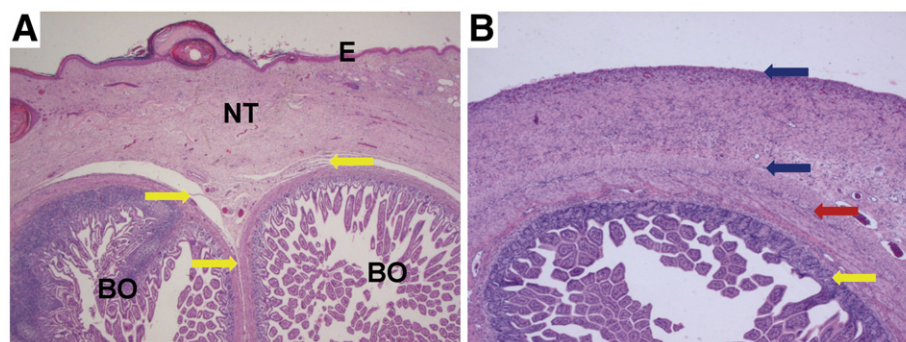


Fig. 4 Histological results of bowel loops. (A) Lambs 1–7, showed a normal appearance, with a normal thin serosa (arrows). BO=bowel loop. NT=newly formed tissue. E=newly formed epidermis. (B) Lamb 8, showed fibrous peel (between blue arrows), slight thickening of the intestinal muscularis (red arrow) and normal mucosa (yellow arrow). (H&E staining, original magnification $\times 25$).

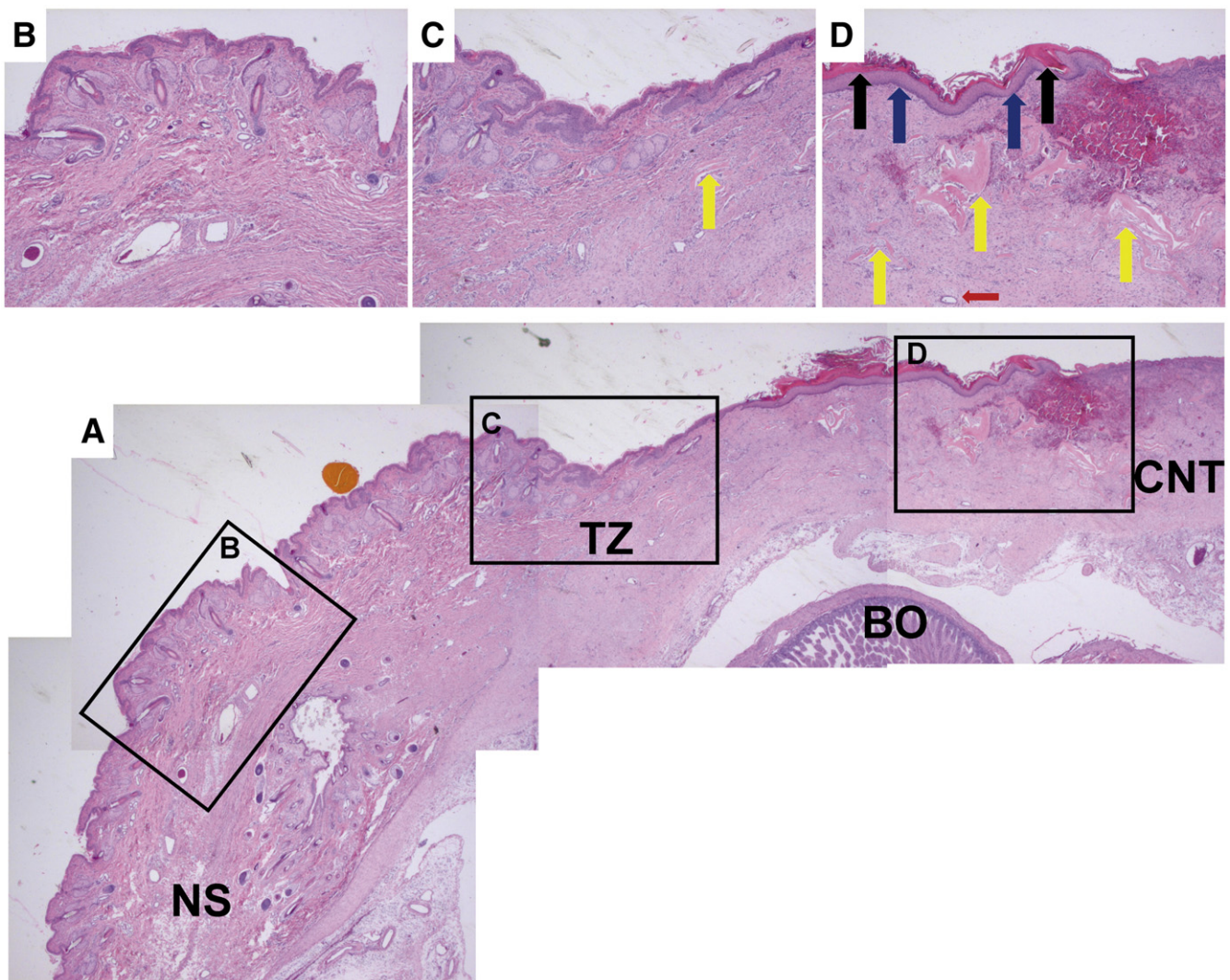


Fig. 5 Histological results of regenerated tissue. (A) Overview of regenerated tissue, showing regenerated skin and connective tissue that replaced the scaffold. NS= native skin tissue and subcutaneous tissue. TZ= transition zone between native tissue and newly formed tissue. CNT= central part of newly formed tissue. BO= bowel loop. (H&E, $\times 12.5$) B, C and D are insets of A (H&E, $\times 25$). (B) Native skin tissue with appendages at the surface. (C) Transition zone between native tissue on the left side and newly formed tissue on the right side. Remnant of the scaffold (arrow). (D) Newly formed skin and subcutaneous tissue at the centre. At the surface hyperkeratinization was visible (black arrows), with hyperplastic epidermis underneath (blue arrows). Remnants of the scaffold were observed in the centre of the tissue (yellow arrows). Capillary (red arrow).

present study, in this previous study the eviscerated bowel was replaced into the abdominal cavity before closure of the abdominal wall. The scaffold was replaced by skin tissue and connective tissue, with good neovascularization and in-growth of smooth muscle cells. No abnormalities of the underlying bowel were seen [20]. In other lambs the bowel had been left eviscerated. In the latter group the bowel resembled human gastroschisis on macroscopic evaluation, i.e. extensive adhesions and fibrous peel formation, and histological evaluation, i.e. a normal mucosa and submucosa, slight thickening of the intestinal muscularis with collagen deposition and fibrous peel formation. The results in this group were comparable to the lamb with the ruptured scaffold in the present study.

In the current study we covered the eviscerated bowel loops with the previously used molecularly defined, biocompatible and biodegradable dual-layer scaffold of highly purified bovine type I collagen. By covering the eviscerated bowel we aimed to prevent fibrous peel and adhesion formation by protecting the bowel against toxic products in the amniotic fluid. Covering the bowel loops instead of closure of the abdominal wall after replacing the bowel loops into the abdominal cavity, as in the previous study [20], will simplify the prenatal operation. For prenatal replacement of the bowel loops into the abdominal cavity the narrow abdominal wall defect needs to be enlarged by a full-thickness incision, and the vulnerable bowel loops, which can already be edematous, thickened and matted, have to be

massaged back into the probably already hypoplastic abdominal cavity [22]. These potentially harmful actions will not be necessary when only covering the eviscerated bowel loops, although an incision in the abdominal wall may still be needed to relieve constriction at the abdominal wall defect. In addition, by using the dual-layer collagen scaffold we aimed to induce cell growth into the scaffold, which ultimately could lead to skin or abdominal wall formation replacing the scaffold, and coverage of the vulnerable eviscerated bowel loops. This would improve postnatal surgical repair when still needed.

The collagen scaffold was sutured into a surgically created skin wound 3 mm from the edges of the abdominal wall defect. This strategy was determined by two considerations. First, in this way the scaffold was not tightly placed around the base of the eviscerated bowel, which is far smaller than the widest diameter of the total package of bowel loops due to the small defect in the abdominal wall. Second, a fresh wound is necessary to induce the repair mechanisms and cellular ingrowth into the scaffold.

In most of the lambs the bowel had returned inside the abdominal cavity at birth. The likely explanation is that slight shrinkage of the scaffold and the growth of the bowel loops has increased pressure in the pocket, allowing the bowel loops to be gradually replaced into the abdominal cavity, mimicking postnatal silo closure in gastroschisis. Skin tissue had formed, and closed the abdominal wall defect. In 2 lambs the bowel loops were still partially outside the abdominal wall, however covered by regenerated skin tissue. In these 2 lambs skin tissue had replaced the collagen scaffold, the extra-abdominal part of the bowel was lying underneath in a subcutaneous pocket. In all but one lamb the bowel appeared normal, without peel formation and with only minor adhesions between bowel loops or with the abdominal wall. The exception was a lamb in which the entanglement of the bowel loops due to adhesions had led to ischemic necrosis and an obstructive ileus. Histology confirmed the normal appearance of the covered bowel loops after birth, without fibrous peel formation or intestinal muscularis thickening. The porous part of the scaffold had been replaced by skin-like tissue and connective tissue.

The film layer was not degraded at birth, and was still visible at the inside of the regenerated tissue. Chemical cross-linking of the collagen and the addition of the film layer, to create a dual-layer scaffold, gave the porous scaffold extra tensile strength [20]. The film layer has less porosity, so cells will not grow into this part of the scaffold. However, due to the low porosity it is presumed to be less or impermeable for toxic products in the amniotic fluid. Additionally, it has higher strength capabilities, and, due to the lower degradability of this layer, the strength of the dual-layer scaffold will be maintained for a longer period. Although the tensile strength of the scaffold was improved, the scaffold had ruptured in one lamb, in which the bowel loops were left uncovered and fibrous peel formation and adhesions were observed. In future research we will combine the collagen

scaffold with a degradable polymer for further improvement of the tensile strength. In addition, improved skin regeneration might be obtained with the application of growth factors to the collagen scaffold, as we demonstrated in a previous study [19].

Prenatal coverage of bowel in gastroschisis with a collagen scaffold is possible in mid-gestation fetal lambs, protecting the bowel loops against toxic waste products in the amniotic fluid. The collagen scaffold is degraded and replaced by skin and connective tissue at birth. In most of the lambs the bowel was repositioned into the abdominal cavity, which may make an extra operation after birth unnecessary. When the bowel still is partially outside the abdominal cavity, like in 2 lambs in the present study, a closure operation will still be needed. However, primary closure may be more straightforward because the bowel will not be thickened or dilated. In addition, this technique provided newly formed skin tissue that can be used during the repair procedure. An obstructive ileus due to adhesions was the only major complication we observed in one lamb, emphasizing the need for careful follow-up when using this technique.

Currently, the major disadvantage of fetal surgery is the risk of complications leading to premature delivery [23,24]. This risk may currently not outweigh the possible benefit for the child born with gastroschisis. However, if intra-uterine coverage of the bowel in gastroschisis is possible with an endoscopic approach, it might become a minimal invasive treatment option for patients with this severe congenital anomaly.

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